8. (Twice Amended) The composition of claim 1, wherein the pH-sensitive polymer is a EUDRAGIT polymer, or a chemical derivative thereof.

9. (Amended) The composition of claim 1, wherein the molecule of interest comprises an active pharmaceutical such as an antimicrobial, antiviral, antiinflammatory, antiseptic, antihistamine, a local anesthetic, a disinfectant, a keratolytic, an analgesic, an anti-migraine, an anti-fungal, a sweetener, a flavoring agent, a diagnostic agent, or combination thereof.

10. (Amended) The composition of claim 1, wherein the molecule of interest is amlexanox.

11. (Amended) The composition of claim 1, wherein the molecule of interest is triclosan.

12. (Amended) The composition of claim 1, wherein the molecule of interest is hirudin.

13. (Amended) The composition of claim 1, wherein the molecule of interest is plasmid DNA.

14. (Amended) The composition of claim 1, wherein the molecule of interest is lidocaine, benzocaine, or dyclonine.

15. (Amended) The composition of claim 1, wherein the molecule of interest is at least one benzodiazepine drug or derivative thereof.

RESPONSE TO OFFICE ACTION

A. Status of the Claims and Specification

Claims 1-32 remain pending. Claims 1-15 have been amended. Claim 1 has been amended simply to incorporate material in the preamble into the body of the claim. Claims 2-15 have been amended to take that change into account. No new matter has been added, and the

amendments conform with all rules applicable to amendments made in response to a final office action.

The substance of all the amendments is illustrated in Appendix A. For the Examiner's convenience, the pending claims, reflecting the amendments made in this response, are attached in Appendix B.

B. Section 103 Rejections

All the pending claims have been rejected as obvious based on the three-way combination of (1) Vora, (2) Acharya, and (3) Benes. These are the same or similar rejections presented during the previous office action. In this section, Applicants reiterate their arguments made in the previous response. In the section after this, Applicants specifically respond to the Examiner's "Response to Arguments."

In view of the amendments and comments of this Response, Applicants respectfully traverse the current Section 103 rejections.

Three basic criteria must be met to establish a *prima facie* case of obviousness:

(1) there must be some suggestion or motivation, either in the References themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;

(2) there must be a reasonable expectation of success; and

(3) the prior art reference (or references when combined) must teach or suggest all the claim limitations.

M.P.E.P. § 2142.

Here, the Office has not established a *prima facie* case, for it has not established any of these three prongs.

1. The references, even when combined, do not teach or suggest all the claim limitations

Even if the three cited references were combined, all of the present claim limitations would not be taught or even suggested.

Claim 1 recites, in part, "a pharmaceutical gel comprising ... at least one pH-sensitive *film-forming polymer forming a film when applied to skin or a mucosal surface* ... ." Independent claim 16 recites, in part, "A pharmaceutical *gel which when applied to the skin or mucosal surface forms a film*, said gel comprising ... at least one pH-sensitive film-forming polymer ... wherein said film is formed due to changes in pH and desolvation of the polymer ... ." (emphasis added). Such features are nowhere taught or suggested in the cited art, taken alone or in any combination.

Vora is directed to a method to treat aphthous ulcers using a paste, solution, gel, and other conventional formulations. [*See* col. 2, lines 42-47]. In contrast to the present invention, Vora nowhere discloses or suggests the use of a pharmaceutical gel utilizing a pH-sensitive film-forming polymer that, when applied to the skin or mucosal surface, forms a film.

Acharya is directed to the use of calcium polycarbophil gels to deliver active agents. [Abstract]. Acharya discloses the formation of a polymeric complex carrier formed by the interaction of calcium and polycarbophil. [Col. 3, lines 15-25]. Specifically, Acharya discloses that the composition is supplied as a two-part system, a polymer phase and a liquid phase. [Col. 3 lines 33-39]. Acharya nowhere discloses or suggests the use of a pharmaceutical gel utilizing a pH-sensitive film-forming polymer that, when applied to the skin or mucosal surface, forms a film.

Benes is directed to the use of a device for the delivery a heparinic anticoagulant across a mucosal surface. [Abstract]. The device includes a reservoir containing a matrix (*i.e.*, a gel,

powder, or tablet containing a heparinic anticoagulant) and an outer mucoadhesive portion. [Figure 1]. The outer mucoadhesive portion is a *pre-formed* solvent-casted film combination of a polymeric resin (*i.e.*, Carbopol) with an elastomeric component. [Col. 5, lines 24-36]. Benes discloses the use of basic (cationic) polyamines such as EUDRAGIT E only to "neutralize" this resin. [Col. 6 lines 13-17]. As evidenced by Figure 1, this pre-formed outer mucoadhesive coating is a pre-casted film (or "sheet") that is subsequently filled with a gel containing a heparinic anticoagulant (*see* Example 1). [*Also*, col. 9 lines 30-67].

Importantly, Benes nowhere teaches the use of a pharmaceutical *gel* including a pH-sensitive film-forming polymer that, *when applied to the skin or mucosal surface, forms a film.* Specifically, the disclosure of a gel residing within a reservoir defined by a pre-formed, neutralized film coating does not amount to the disclosure or even suggestion of a gel composition including a component that, upon application to the skin or mucosal surface, itself forms a film. In fact, it can be argued that the disclosure of Benes teaches away from such a concept because it effectively teaches the advantages of using a pre-formed film or sheet with a backing to create a gel-filled reservoir. [*See* Figure 1].

The Office's present arguments appear to be an improper piecing-together of disparate elements from different references. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 230 U.S.P.Q. 416 (Fed. Cir. 1986) ("It is impermissible within the framework of 35 U.S.C. § 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art."). For example, the Office argues that the film-forming component of the presently-recited gel is contained in Benes, when in fact, Benes simply mentions that Eudragit can be used to neutralize a resin within a pre-formed sheet. [Col. 6, lines 13-17; *also*

Figure 1]. The mere naming of Eudragit in the Benes reference (in a different context) does not establish the claimed elements, nor does it advance any basis for obviousness under an "inherency" theory. *In re Newell*, 13 U.S.P.Q.2d 1248 (Fed. Cir. 1989) ("[A] retrospective view of inherency is not a substitute for some teaching or suggestion *which supports the selection and use of the various elements in the particular claimed combination.*") (emphasis added).

Accordingly, none of the cited teaches or even suggests the elements required by the pending claims — particularly a gel composition that forms a film when applied to skin or a mucosal surface. Thus, there can be no *prima facie* case of obviousness, and the pending claims are accordingly in condition for allowance.

2. *There is no suggestion or motivation to modify the references or to combine the reference teachings*

In order for the cited references to even arguably be pertinent, one of ordinary skill in the art would have to significantly modify Benes, which discloses that EUDRAGIT is used simply to neutralize a pre-formed outer film layer that encases a reservoir of gel. [Col. 6 , lines 13-17; *also*, Figure 1]. In particular, Benes would have to modified so that the EUDRAGIT, instead of simply neutralizing the pre-formed outer coating, would instead be appropriately combined in a particular gel composition in such a way that a film would form upon application to the skin or mucosal surface. [*See, e.g.*, independent claims 1, 16]. No such motivation exists (or is cited by the Office) for this modification. Further, such a modification would change the operation of Benes — instead of utilizing a pre-formed film encasing a reservoir, Benes would operate by utilizing a gel that itself formed a film upon application. Accordingly, this modification is improper. *See* M.P.E.P. 2143.01 ("If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the

teachings of the references are not sufficient to render the claims prima facie obvious."). The claims are therefore in condition for allowance.

3. The Office has not established that there would be a reasonable expectation of success

The Office has not shown or argued the required reasonable expectation of success. Applicants respectfully submit that there is nothing in the cited art that demonstrates a reasonable expectation of success surrounding the significant modification of Benes discussed above. In particular, there is nothing in the record to suggest that the abandonment of the pre-formed film encasing a gel in Benes in favor of a different gel composition including a film-forming polymer that forms a suitable film upon application to the skin or mucosal surface would be successful. Accordingly, for this reason as well, the claims are not *prima facie* obvious and should be allowed to issue.

B. Applicants' Answer to "Response to Arguments"

In the first paragraph of the "Response to Arguments" section, the Examiner argues that:

1) Vora teaches using a gel;
2) Acharya teaches films being used to contact mucosal or skin surfaces;
3) Benes teaches the administration of drugs across mucosal surfaces.

The Examiner concludes that the art meets the limitations of claim 1. Applicants respectfully traverse. The references clearly lack disclosure or suggestion of the particular gel of claim 1 – a pharmaceutical gel including at least one pH-sensitive film-forming polymer forming a film when applied to skin or a mucosal surface. Likewise, the gel of claim 16 is not disclosed or suggested. Separate recitations of films, drugs, and gels do not amount to the disclosure or suggestion of such a particular gel. Applicants have not improperly attacked references

individually. Again, *none* of the references disclose or suggest such a gel. Thus, even in combination, a *prima facie* case for obviousness has not been met.

In the second paragraph of the "Response to Arguments" section, the Examiner argues that:

1) Benes does not need to modified to meet the claims;
1) Benes teaches a matrix, which can be a gel;
2) Benes teaches means for maintaining the matrix in contact with a mucosal surface;
3) The means include resins containing coboxylic acid moieties; and
4) Benes meets the claims because it is "drawn to a gel-formed delivery device that can consist of Eudragit."

Applicants respectfully traverse. The Examiner's position is that any "gel-formed delivery device that can consist of Eudragit" renders the claims obvious. This is in error. The claims are not that broad, nor do they purport to be. Claim 1 recites a gel that includes at least one pH-sensitive film-forming polymer forming a film when applied to skin or a mucosal surface. Claim 1 has been amended so that the subject "gel" composition is in the body of the claim, not the preamble. Thus, it is even more clear that the present invention contemplates a particular gel composition that, due to its composition, forms a film when applied to skin or a mucosal surface. Claim 16 is similar. Disclosure of a pre-formed outer mucoadhesive coating that is subsequently filled with a separate gel, as done in Benes, simply does not amount to a disclosure or even a teaching of such a gel. Benes would have to be significantly modified to change the composition of its gel "matrix" so that such gel would include additional materials to ensure that a film be formed when applied to skin or a mucosal surface. Motivation for that modification is lacking.

In the third paragraph of the "Response to Arguments" section, the Examiner argues that Benes requires no modification. Applicants respectfully traverse. Again, Benes would have to be changed so that its gel were different to ensure that it would form a film when applied to the skin or mucosal surface. The Examiner has not shown why such a modification would have a reasonable expectation of success.

In sum, while Applicants appreciate the Examiner's explanation of rejections, they respectfully traverse the reasoning and assertions given in support thereof. The cited references do not disclose or suggest, alone or in combination, the features of the pending claims. The claims are in condition for allowance, and favorable reconsideration is respectfully requested.

CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so the claims may swiftly pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3018 is respectfully requested in advance.

Respectfully submitted,

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APPENDIX A -- AMENDMENTS

In the Claims:

1. (Twice Amended) A [pharmaceutical gel] composition comprising:

a pharmaceutical gel comprising:

a solvent vehicle,

at least one water-insoluble swellable mucoadhesive polymer,

at least one pH-sensitive film-forming polymer forming a film when applied to skin or a mucosal surface, and

at least one molecule of interest.

2. (Amended) The [gel] composition of claim 1, wherein the solvent vehicle is comprised of at least 25 to 100 parts water or buffered water with 0 to 75 parts of ethanol, propylene glycol, glycerin, polyethylene glycol, or combinations thereof.

3. (Amended) The [gel] composition of claim 1, wherein the water-insoluble swellable mucoadhesive polymer is polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol.

4. (Twice Amended) The [gel] composition of claim 1, wherein the water-insoluble swellable mucoadhesive polymer is NOVEON or CARBOMER.

5. (Amended) The [gel] composition of claim 1, wherein the water-insoluble swellable mucoadhesive polymer is present at a concentration of from 0.1% to 20% by weight.

6. (Amended) The [gel] composition of claim 1, wherein the pH-sensitive polymer is a copolymer of methacrylic acid and acrylic or methacrylic ester.

7. (Amended) The [gel] composition of claim 1, wherein the pH-sensitive polymer is present at a concentration of from 0.05% to 10% by weight.

8. (Twice Amended) The [gel] composition of claim 1, wherein the pH-sensitive polymer is a EUDRAGIT polymer, or a chemical derivative thereof.

9. (Amended) The [gel] composition of claim 1, wherein the molecule of interest comprises an active pharmaceutical such as an antimicrobial, antiviral, antiinflammatory, antiseptic, antihistamine, a local anesthetic, a disinfectant, a keratolytic, an analgesic, an anti-migraine, an anti-fungal, a sweetener, a flavoring agent, a diagnostic agent, or combination thereof.

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12. (Amended) The [gel] composition of claim 1, wherein the molecule of interest is hirudin.

13. (Amended) The [gel] composition of claim 1, wherein the molecule of interest is plasmid DNA.

14. (Amended) The [gel] composition of claim 1, wherein the molecule of interest is lidocaine, benzocaine, or dyclonine.

15. (Amended) The [gel] composition of claim 1, wherein the molecule of interest is at least one benzodiazepine drug or derivative thereof.